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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/516,728	03/01/2000	Thomas O Daniel	1242/12/2	2723

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	27

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/516,728	DANIEL ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *26* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/2003 has been entered.

2. Claims 1-55 are canceled without prejudice or disclaimer, claims 56-89 are newly added.

3. Claims 56-89 are therefore pending and examined on the merits.

Information Disclosure Statement

4. The Information Disclosure Statement filed 9/22/2003 (paper no. 26) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 56-89 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 56-89, as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph

7. Claims 74-75, 80 and 89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 74-75, 80 and 89 recite specific cell lines.

It is apparent that the recited cell lines are required to practice the claimed invention, because they are specifically required in the claims. As required elements they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first

paragraph, may be satisfied by a deposit of the cell lines listed in claim 7. See 37 CFR 1.802.

While the specification states on page 42 that the cell lines have been deposited for patent purposes, the specification does not indicate the terms of the deposit.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 56-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following is noted.

The specification disclosed that the sequence set forth in Ostman *et al* (PNAS US 1994;91:9680-9684) was used as the immunizing antigen for the production of the claimed antibodies. Such incorporation by reference is improper. The claims are not

enabled, because one of ordinary skill in the art could not make or use the invention with any predictability because the claims do not specifically limit the amino acid sequence of the DEP-1 protein nor does it provide specific sequence information for the DEP-1 protein. The disclosed amino acid sequence must be made part of the instant application.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries

or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the making of the antibody using any DEP-1 protein would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant is reminded to provide said Sequence Listing which complies with the requirements of 37 CFR 1.821 through 1.825 for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is reminded to provide the appropriate Hawkins Declaration to accompany amending the instant specification to provide the essential subject of the "amino acid sequence" defining the claimed "antigen", as set forth by Ostman *et al.*

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 56,62,68-69,73,76-77, and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Honda H *et al* (Blood 1994 Dec;81(12):4186-4194, IDS C1 filed 6/20/00). Claims are drawn to an antibody which binds to an epitope within amino acids 175-536 of human ECRTP/DEP-1 polypeptide (herein referred to as DEP-1), wherein the antibody is in a pharmaceutically acceptable diluent or excipient; an antibody, fragment or derivative thereof which specifically binds an extracellular domain of DEP-1 polypeptide and angiogenesis modulating activity, wherein the antibody, fragment or derivative thereof has activity in modulating angiogenesis in an assay, and wherein the said antibody is in a pharmaceutically acceptable diluent or excipient; an antibody, fragment or derivative thereof which specifically binds to an epitope within amino acids 175-536 of human DEP-1 and has angiogenesis modulating activity, wherein said antibody has activity in modulating angiogenesis in an assay, and wherein the said antibody is in a pharmaceutically acceptable diluent or excipient.

Honda *et al* disclose an antibody that is generated from a peptide fragment within amino acids 175-536 (see page 4187 "E*xpression of extracellualr region and generation*

of antibody"), wherein primers corresponding to nucleotide 1131-1152 and 1838-1859 where used to generate the immunizing peptide corresponding to amino acids 293-536 of human DEP-1. Because the antibody generated was derived from rabbit serum, it is already in a pharmaceutically acceptable carrier. Furthermore, because the antibody taught by Honda *et al* was generated within the same region as that instantly claimed, and although Honda *et al.* do not characterize antibody as having angiogenesis modulating activity, the claimed functional limitation would be an inherent property. Thus, it does not appear that the claim language or limitation results in a discernable difference in the antibody when compared to the prior art disclosure.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 56-58, 60-62, 68-73, 76-79, and 81-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Honda *et al* (cited above) in view of Tonks *et al* (WO 95/30008, IDS B2 filed 6/20/00). Claims 56,62,68-69,73,76,77,and 82 are discussed above. Claims 57, 70 and 78 are further limiting the said antibody to fragments selected from the group consisting of Fab, Fab', F(ab')2, Fv, and scFv. Claims 58, 71, and 79

are further limiting the said antibody to a monoclonal antibody or fragments or derivatives thereof. Claims 60, 72, and 81 are further limiting the said antibody to a humanized antibody.

The Honda *et al* reference, as discussed *supra*, does not specifically characterize the antibody as fragments, monoclonal or as being in humanized form. This deficiency is remedied by Tonks *et al*.

Tonks *et al* teaches the discovery of DEP-1 protein and further discusses the production of antibodies to the DEP-1 polypeptide. Among the different types of antibodies, Tonks *et al* specifically discloses monoclonal antibodies, Fab fragments, and chimeric antibodies (see page 8, lines 17-22).

Therefore, it would have been *prima facie* obvious at the time the invention was made to one of ordinary skill in the art to produce DEP-1 monoclonal antibodies, fragments of DEP-1 antibodies such as Fab fragments, and humanized forms of DEP-1 antibodies. One of skill in the art would have found motivation in doing so because DEP-1 had been found to be a PTPase that may be important in signal transduction, and that Tonks *et al* disclosed that modulation of such PTPase activity can be accomplished by using antibodies to the DEP-1 wherein the antibodies could be in the form of monoclonal, fragments, and chimeric antibodies. One of skill in the art would have expected a reasonable amount of success in manipulating the antibody of Honda *et al* into fragments or humanized versions because such techniques where already well established in the art as possible modification of base antibodies that are functionally active. It is also well known in the art that humanized antibodies are chimeric antibodies

between mouse CDR regions and human framework. Furthermore, one of ordinary skill would have found reasonable expectation of success in making monoclonal antibodies based on the finding of the polyclonal antibody discussed by Honda *et al* because the peptide used in the immunizing the rabbit could have been easily injected into a mouse to generate the monoclonal form of the DEP-1 antibody.

Therefore, given the findings of Honda *et al* in view of the motivation by Tonks *et al*, one of ordinary skill would have found it obvious to make an antibody to DEP-1 using a peptide derived from DEP-1 amino acids 175-536, wherein the antibody is monoclonal, fragments, and humanized.

Conclusion

No claims are allowed. Claims 61, 63-67, 74-75, 83-89 appear to be free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary Nickol for:

Christopher Yaen
Art Unit 1642
December 4, 2003